POLYNUCLEOTIDE SAMPLE PREPARATION DEVICE

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] The present application claims the benefit of priority of U.S. provisional application Ser. No. 60/726,066, filed Oct. 11, 2005, the specification of which is incorporated herein by reference in its entirety.

TECHNICAL FIELD

[0002] This technology described herein relates to methods and devices for preparing polynucleotide-containing samples, and more particularly to methods and devices that utilize microfluidic components for preparing samples for subsequent analysis of polynucleotides contained therein.

BACKGROUND

[0003] Many laboratory techniques involve detection, quantitative analysis, or amplification of polynucleotides. For example, the polymerase chain reaction (PCR) is a well-established routine laboratory practice for amplifying DNA in DNA-containing samples. Nevertheless, even routine practices would benefit from levels of automation that would increase throughput, improve consistency of analyses, and be simple to use, as well as save processing and analysis time for individual samples.

[0004] One aspect in which the overall time of an analysis, such as PCR, can be significantly shortened, without a detrimental impact on reliability, is the initial processing of the nucleotide-containing sample. Since analytical techniques such as PCR have already been subject to certain levels of automation within the industry, there exists a need to develop efficient means of sample preparation that provides DNA extracts from raw clinical samples in a form that can be immediately input to existing machines.

[0005] For analytic methods such as PCR to be effective, individual DNA molecules must be liberated from their host cell nuclei. Thus, in cell-containing samples, cell walls, and nuclear membranes must both be ruptured to permit DNA molecules to enter the surrounding milieu. Overall, several steps are typically required to extract useable DNA from a cell-containing sample. Development of a simple device that can carry out such steps routinely and efficiently would be of considerable benefit to, for example, those who carry out existing PCR protocols, not least because existing attempts at automation have involved complex and expensive technologies, such as robotics.

[0006] Microfluidics has proven to be a practical technology for carrying out both sample preparation for diagnostic analysis, and analysis of micro-liter scale samples by methods such as PCR. See, for example, PCT application no., PCT/US2005/015345, and U.S. provisional application Nos. 60/567,174, and 60/645,784, all of which are incorporated herein by reference in their entirety. However, to date, a tool that has not been developed is a microfluidic component that can deliver nucleotide samples in a form that can be conveniently analyzed by existing laboratory equipment, including the thermal cyclers used in PCR.

[0007] Microfluidic devices with various components are described in U.S. provisional application No. 60/553,553 filed Mar. 17, 2004 by Parunak et al., which is incorporated herein by reference.

SUMMARY

[0008] Systems as described herein include a microfluidic system for converting a sample containing one or more polynucleotides into a form suitable for analyzing the one or more polynucleotides, the system comprising: a cartridge receiving element in communication with an insertable and removable cartridge; a heating element in communication with the cartridge receiving element, configured to heat one or more regions of the cartridge; and control circuitry in communication with the heating element; wherein the insertable cartridge comprises: at least one microfluidic component that, in conjunction with the heating element and the control circuitry, is configured to accept the sample and one or more reagents, and to react the sample and the reagents, in order to produce a prepared sample suitable for analysis of the one or more polynucleotides.

[0009] In other embodiments, the insertable cartridge further comprises: a sample inlet for receiving the sample; a reagent inlet for accepting one or more reagents; and an outlet for directing prepared sample into a PCR tube. In still other embodiments, the microfluidic component comprises: one or more channels configured to transmit volumes of fluid in the range 0.1-50 μl, wherein the one or more channels ensure passage of sample, reagents, and fluid between the sample inlet, the reagent inlet, and the outlet.

[0010] The prepared sample produced by the microfluidic system as further described herein can be subsequently analyzed by a machine configured to carry out a method selected from the group consisting of: PCR, TMA, SDA, and NASBA. The prepared sample produced by the microfluidic system may be further processed and analyzed by a variety of target amplification and/or signal amplification techniques and may also be analyzed by restriction digestion followed by capillary electrophoresis and/or mass spectrophotometry analysis, and other examples of techniques commonly referred to as genomic and proteomic technologies.

[0011] Preferred embodiments of the microfluidic system further comprise one or more components of computing machinery, such as: a visual display that communicates to a user of the system information including the current status of the system, progress of sample preparation, and a warning message in case of malfunction of either system or cartridge; an interface for connecting the system to a computer or a network of computers; a computer-readable memory which stores instructions for operating the control circuitry; a processing unit for executing the instructions; and an input device for accepting information from a user.

[0012] Other preferred embodiments of the system described herein utilize a cartridge that is configured to accept two or more separate samples. Still other preferred embodiments of the system are configured to accept two or more cartridges, preferably three cartridges, any one cartridge of which is configured to accept two or more separate samples.

[0013] Also further described herein are embodiments of a microfluidic component for converting a sample containing one or more polynucleotides into a form suitable for analyzing the one or more polynucleotides, the component comprising: a sample inlet for receiving the sample; a reagent inlet for accepting one or more reagents; an outlet